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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,539	07/01/2003	Bansi Lal	516745-2001.1	4710

7590 04/19/2006

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EXAMINER	
KOSACK, JOSEPH R	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,539	LAL ET AL.	
	Examiner	Art Unit	
	Joseph Kosack	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) *14-22* is/are withdrawn from consideration.

5)☒ Claim(s) *4,5,7,11 and 24* is/are allowed.

6)☒ Claim(s) *8,12,13,25 and 26* is/are rejected.

7)☒ Claim(s) *1-3,9 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-22, 24-26 are pending in the instant application.

Amendments

The amendments filed on February 3, 2006 and February 10, 2006 have been acknowledged and have been entered into the record.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-13, along with an election of species of Compound 12 from the specificaion in the reply filed on August 4, 2005 was acknowledged in the action mailed on November 4, 2005. The restriction has been traversed again in the replies of February 3, 2006 and February 10, 2006. The traversal is on the ground(s) that the search of the entire scope of the invention would not be unduly burdensome. This is not found persuasive because a search of the entire scope of the invention turned up over 2,000 unique references:

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  8.3% PROCESSED     2000 ITERATIONS                                2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       475446 TO   494074
PROJECTED ANSWERS:             189 TO      779

L7            2 SEA SSS SAM L6

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FULL SEARCH INITIATED 15:31:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   486164 TO ITERATE

100.0% PROCESSED   486164 ITERATIONS                             727 ANSWERS
SEARCH TIME: 00.00.04

L8          727 SEA SSS FUL L6

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                   166.94     434.39

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=> 18
L9        2644 L8

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PROCESSING IS APPROXIMATELY  82% COMPLETE FOR L9
PROCESSING COMPLETED FOR L9
L10        2477 DUP REM L9 (167 DUPLICATES REMOVED)
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This leads to a definitive conclusion of undue burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

In the previous action, claims 1-13 were examined for patentability. Claims 1-3 and 12 were rejected under 35 U.S.C. 102(b) as being anticipated by Gross et al. and Mansuri et al. Claims 5, 7-10, and 13 were objected to. In the amendments, claims 6 and 23 have been cancelled and claims 24-26 have been added. Claims 24-26 will be combined with Group I and will be examined for patentability. Claims 14-22 remain withdrawn as being drawn to a non-elected invention. The generic concept examined in the action mailed on November 4, 2005 remains unchanged.

Claim Objections

Claims 1-3, 9-10, 12-13, and 25-26 are objected to for containing elected and non-elected subject matter. The elected subject matter have been identified in the action mailed on November 4, 2005.

Previous Claim Rejections - 35 USC § 102

In the previous action mailed on November 4, 2005, claims 1-3 and 12 were rejected under 35 U.S.C. 102(b) as being anticipated by Gross et al. and Mansuri et al. Applicant has correctly cited that the references do not teach the requirement that the A ring must be substituted by one R_6 unit that can only be -C_1-C_4-alkyleneOR_{11} unit. Therefore, due to Applicant's arguments, the rejections under 35 U.S.C. 102(b) are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-13 and 25-26 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of certain cancers, does not reasonably provide enablement for all cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention are pharmaceutical compositions comprising the compound of formula 1c with a pharmaceutically acceptable carrier with the intended use for the treatment of disease mediated by inhibition of cyclin dependent kinase (Claims 12-13) or excessive cell proliferation (Claims 25-26).

The State of the Prior Art and the Predictability or Lack Thereof in the Art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what

compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:
It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Davies et al. (*Pharmacology & Therapeutics, 2002*, 125-133) and Toogood (*Medicinal Research Reviews, 2001*, 487-498) both teach various inhibitors of CDK2 and CDK4, but show no data as to the usefulness of inhibiting these kinases as a treatment for cancer.

Hence, in the absence of a showing of correlation between all cancers claimed as capable of treatment by inhibiting cyclin dependent kinases, one of skill in the art is unable to fully predict possible results from the administration of the compound of formula 1c due to the unpredictability of the role of inhibiting cyclin dependent kinases, and the unpredictability of the ability of the compound of formula 1 to cause toxicity or any improvement in condition.

The Amount of Direction or Guidance Present and the Presence or Absence of Working Examples

The specification teaches in vitro assays done on two compounds of the instant invention with 6 different cell lines: HeLa Cervix, MCF-7 Breast, PC-3 Prostate, MDAMB-231 Breast, H460 Lung, and U-937 Histiocytic lymphoma (monocytes). If activity is to be judged by the toxicity of the compounds to the different cell lines, it seems to the Examiner that the compounds contain no activity towards MDAMB-231 Breast and H460 Lung cell lines, since the definition of "not toxic" is less than or equal to 30% toxic, which would include 0% toxicity. The compounds do contain activity to the other four cell lines, providing sufficient guidance to those of skill in the art to practice the invention to the scope of the intended use for the treatment of those specific cancers.

The Breadth of the Claims

The breadth of the claims are pharmaceutical compositions comprising the compound of formula 1c with a pharmaceutically acceptable carrier with the intended use for the treatment of all disease mediated by inhibition of cyclin dependent kinase (Claims 12-13) or excessive cell proliferation (Claims 25-26).

The Quantity of Experimentation Needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine which cancers can be treated with the compounds of the instant invention, dosages, the method of drug delivery, and any potential combination therapies.

The Level of Skill in the Art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad intended use of the compound of formula 1c for the treatment of all diseases mediated by cyclin dependent kinases or excessive cell proliferation. As a result, necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of formula 1c in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome deleting the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 contains in the definition of substituent A the definition "wherein X_1 is a carbon atom or and," leading one of skill in the art to believe that X_1 could be carbon or any other atom, hence an indefinite number of compounds.

Conclusion

Claims 8, 12-13 and 25-26 are rejected. Claims 1-3, 9-10, 12-13, and 25-26 are objected to. Claims 4-5, 7, 11, and 24 are held to be allowable. All examined claims are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-F 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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